	MHC-II	MHC-II	MHC-II	MHC-II
MHC Haplotype H-2 <sup>b</sup> (C57BL/6 mice)	I-A <sub>α</sub> <sup>b</sup>	$I$ - $A_{\beta}$ <sup>b</sup>	$(I-E_{\alpha}{}^{b} not$	$I$ - $E_{\beta}{}^{b}$
Functional MHC-II available in H-2 <sup>b</sup>	$I-A_{\alpha}{}^{b}I-A_{\beta}{}^{b}$		No I-E available in H-2 <sup>b</sup>	
MHC Haplotype H-2 <sup>k</sup> (CBA mice)	I-A <sub>α</sub> <sup>k</sup>	$I-A_{\beta}^{k}$	I-E <sub>α</sub> <sup>k</sup>	$I$ - $E_{\beta}^{k}$
Functional MHC-II available in H-2 <sup>k</sup>	$I-A_{\alpha}{}^kI-A_{\beta}{}^k$		$I-E_{\alpha}{}^{k}I-E_{\beta}{}^{k}$	
H-2 <sup>b/k</sup> (C57BL/6 x CBA)	I-A <sub>α</sub> <sup>b</sup>	$I$ - $A_{\beta}^{b}$	$(I-E_{\alpha}{}^{b} \text{ not present})$	$I$ - $E_{\beta}{}^{b}$
	$I-A_{\alpha}^{k}$	$I-A_{\beta}^k$	I-E <sub>α</sub> <sup>k</sup>	$I\text{-}E_{\beta}{}^{k}$
	Not only	I-A <sub>α</sub> <sup>b</sup> I-	I-A <sub>α</sub> <sup>k</sup>	I-E <sub>α</sub> <sup>k</sup>
Functional MHC-II available in H-2 <sup>b/k</sup>		$A_{eta}^{b}$	$I-A_{\beta}^{k}$	$I$ - $E_{\beta}^{k}$
	But also	$I-A_{\alpha}{}^{b}I-$ $A_{\beta}{}^{k}$	$I-A_{\alpha}{}^{k}$ $I-A_{\beta}{}^{b}$	I-E <sub>α</sub> <sup>k</sup> I-E <sub>β</sub> <sup>b</sup>

**S2 Table.** Why there are more variants of MHC-II restricting molecules available in C57BL/6 x CBA F1 mice than in C57BL/6 or CBA mice? A promoter mutation disrupts production of I-E $\alpha^b$  in C57BL/6 mice (Grey font), which are therefore unable to produce MHC-II I-E (Grey). In contrast, H-2<sup>k</sup> mice can produce both I-A $\alpha^k$  I-A $\alpha^k$  and I-E $\alpha^k$  I-E $\alpha^k$ . C57BL/6 x CBA F1 mice have an even bigger repertoire of possible functional MHC-II isoforms available due to heterodimerization of  $\alpha$  and  $\beta$  subunits from H-2<sup>b</sup> and H-2<sup>k</sup> haplotypes.